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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/663,158	09/15/2003	Frederic DeSauvage	11669.123USC1	4053

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EXAMINER	
RINAUDO, JO ANN S	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 11/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/663,158	DESAUVAGE ET AL.	
	Examiner	Art Unit	
	Jo Ann Rinaudo	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *1-14,17-22 and 26-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15,16 and 23-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-34 are pending.

2. Applicant's election with traverse of Group X (Claims 15, 16, and 23-25) in a reply filed on 19 September 2005 is acknowledged. The traversal is on the grounds that it would not be unduly burdensome for the Examiner to search and examine all the claims directed to a method of preventing, inhibiting, or attenuating the differentiation of T-cells into the Th2 subtype regardless of the particular agonist used. This is not found persuasive because the T-cell agonists recited in the claims are small molecules, antibodies, and a stable TCCR ECD. These products are distinct because their structures, physicochemical properties, and/or the mode of action are different, and they do not share a common structure that is disclosed to be essential for common utility. Therefore, a method of preventing, inhibiting, or attenuating the differentiation of T-cells into the Th2 subtype differ with respect to ingredients and method steps. Further, a prior art search also requires a literature search and as such, would impose an undue burden on the Examiner.

3. The requirement is still deemed proper and is therefore made FINAL.

4. Claims 1-14, 17-22, and 26-34 are withdrawn from further consideration by the Examiner, under 37 C.F.R. § 1.142(b), as being drawn to nonelected inventions.

5. Claims 15, 16, and 23-25 are under consideration as they are drawn to a method of preventing, inhibiting, or attenuating the differentiation of T-cells into the Th2 subtype comprising administering a TCCR agonist, wherein the preventing, inhibiting, or attenuating occurs in a mammal; wherein the agonist is a monoclonal antibody, an antibody fragment, or a single-chain antibody, and wherein the antibody has nonhuman complementarity determining region (CDR) residues and human framework (FR) residues.

6. The specification, on page 48, lines 12-18 discloses that the full-length native sequence TCCR gene described in FIG 3. (SEQ ID NO:1) and FIG. 4 (SEQ ID NO:2). Figures 3 and 4 and

SEQ ID NO: 1 and SEQ ID NO:2 are amino acid sequences, not DNA sequences. SEQ ID NO: 3 and SEQ ID NO: 4 are DNA sequences. Correction is required.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 15, 16, and 23-25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

9. The specification does not appear to provide sufficient guidance for a method of preventing, inhibiting, or attenuating the differentiation of T-cells into the Th2 subtype comprising administration of an effective amount of an agonist TCCR antibody, fragment or single chain antibody, wherein the preventing, inhibiting, or attenuating occurs in a mammal.

10. Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the amount of direction or guidance provided, the lack of sufficient working examples, and the amount of experimentation required to enable one skilled in the art to practice the invention.

11. The specification fails to provide guidance for using agonist TCCR antibodies in a method of preventing, inhibiting, or attenuating the differentiation of T-cells into the Th2 subtype, wherein the preventing, inhibiting, or attenuating occurs in a mammal. The only *in vivo* model in the specification discloses TCCR "knockout" Mice (see Example 2, pages 87-88, in particular) and further that TCCR -/- mice have a greater Th2 response (see Example 3, page 89, lines 6-7, in particular). In addition, the specification discloses that *in vitro* cultures of CD4+ cells from spleen and lymph nodes of TCCR deficient mice have a diminished Th1 response and an enhanced Th2 response (see Example 12, page 105, lines 1-3 and 19-33, in particular). The specification provides no examples of the use of agonist antibodies *in vivo* in a method of

preventing, inhibiting, or attenuating the differentiation of T-cells into the Th2 subtype. Several cyokines are involved in the differentiation of T-cells into the Th2 subtype. Paul teaches that the differentiation of T-cells into the Th2 subtype is induced by IL-4 (see page 735, column 1, paragraph 3, in particular). Further, Paul teaches that IL-4 acts through two receptors on T-cells (see page 716, column 1, *Two Types of IL-4 Receptors*, in particular). Therefore, it is unclear how agonist TCCR antibodies could prevent differentiation of T-cells into the Th2 subtype in a mammal, if other cytokines are also involved in this process. Consequently it would require undue experimentation of the skilled artisan to establish a method of preventing, inhibiting, or attenuating the differentiation of T-cells into the Th2 subtype comprising administration of an effective amount of an agonist TCCR antibody, fragment or single chain antibody, wherein the preventing, inhibiting, or attenuating occurs in a mammal.

12. The specification provides no guidance for a method of "preventing" the differentiation of T-cells into the Th2 subtype comprising administration of an effective amount of a TCCR agonist antibody in a mammal (Claims 15 and 16). The word "prevent" is defined as "keep from happening or existing" (Merriam-Webster Online Dictionary). The claim, as recited, would have to contact ALL the T-cells in a mammal and STOP ALL the T-cells from differentiating into the Th2 subtype in a mammal. Therefore the skilled artisan cannot envision a method of "preventing" the differentiation of T-cells into the Th2 subtype comprising administration of an effective amount of a TCCR agonist antibody in a mammal (Claims 15 and 16).

13. The recitation of a "TCCR polypeptide or agonist thereof" (Claim 15); wherein the "agonist is a monoclonal antibody" (Claim 23), and an "antibody fragment" (Claim 25) are not commensurate with the disclosure in the specification. The specification only provides the amino acid sequences of two TCCR polypeptides, SEQ ID NO:1 and SEQ ID NO:2 which can be used to produce monoclonal antibodies specific for SEQ ID NO:1 or SEQ ID NO:2. In addition, the term "antibody fragment" is defined in the specification as "comprise a portion of an intact antibody, preferably the antigen binding or variable region of the intact antibody" (see page 27, lines 28-29, in particular). It is well established in the art that the Fc fragment of an antibody is a fragment of an antibody that cannot bind an antigen (see Benjamini et al.). Therefore the skilled artisan cannot envision all the possible TCCR monoclonal antibodies or

antibody fragments, other than monoclonal antibodies or fragments thereof which specifically bind SEQ ID NO:1 or SEQ ID NO:2.

14. The specification does not provide a sufficient enabling description of a TCCR "agonist" (Claim 15). A person of skill in the art is not enabled to make and use ANY "agonists" TCCR encompassed by the full breadth of the claims. The term "agonist" as recited encompasses ANY molecule that "mimics, enhances or stimulates the biological activity of a native sequence of TCCR polypeptide of the invention disclosed herein" (see page 26, lines 9-11, in particular). Molecules having highly diverse structural and biochemical properties can function as "agonists" and "antagonists". Huang teaches the daunting task faced by the skilled artisan in developing small molecule regulators of protein-protein interactions, and notes that the process required long periods of trial and error testing before suitable compounds could be developed (see page 202, "Introduction", in particular). Therefore, the skilled artisan cannot envision how to make and use all the possible TCCR "agonists", other than monoclonal antibodies or fragments thereof which specifically bind SEQ ID NO:1 or SEQ ID NO:2.

15. Claim 24 recites the "antibody has nonhuman complementarity determining region (CDR) residues and human framework region (FR) residues". It is well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody. Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al. (see entire document and page 1980 column 1, lines 28-52 and column 2, lines 1-38, in particular). Therefore, the skilled artisan cannot envision all the possible "nonhuman complementarity determining region (CDR) residues and human framework region (FR) residues" in the TCCR antibody which specifically binds SEQ ID NO:1 or SEQ ID NO:2.

16. Reasonable correlation must exist between the claims and the enablement set forth. In view of the quantity of experimentation necessary, the limited working examples, the nature of the invention, the state of prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

17. Claims 15, 16, and 23-25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

18. There is insufficient written description in the specification for a method of "preventing" the differentiation of T-cells into the TH2 subtype, in a mammal (Claims 15 and 16). The specification only discloses the antibodies may be used to treat various immune related diseases and conditions, such as T cell mediated diseases (see pages 77-84, Methods of Treatment, in particular). Therefore, the skilled artisan cannot envision a method of "preventing" the differentiation of T-cells into the TH2 subtype in a mammal.

19. There is insufficient written description of a method of preventing, inhibiting, or attenuating the differentiation of T-cell into the Th2 subtype, comprising administration of a TCCR "agonist" (Claim 15). The specification does not disclose the structural and functional properties associated with a TCCR "agonist". Therefore, the skilled artisan cannot envision all the contemplated TCCR "agonists" used in a method of preventing, inhibiting, or attenuating the differentiation of T-cell into the Th2 subtype.

20. There is insufficient written description in the specification for a method of "preventing" the differentiation of T-cells into the Th2 subtype. The specification does not disclose the structural and functional properties associated with a TCCR agonist monoclonal antibodies or antibody fragments (Claims 15, 23 and 25) or an antibody that has nonhuman complementarity determining region (CDR) residues and human framework region (FR) residues (Claim 25). The specification has only discloses the specific TCCR with SEQ ID NO:1 and SEQ ID NO: 2 that can be used as an antigen to produce monoclonal antibodies. Therefore, other than monoclonal antibodies, fragments thereof that bind specifically to SEQ ID NO:1 and SEQ ID NO: 2, the skilled artisan cannot envision all the contemplated TCCR agonist monoclonal antibodies, antibody fragments, or an antibodies that have nonhuman complementarity determining region (CDR) residues and human framework region (FR) residues.

21. Consequently, conception cannot be achieved until a representative description of the

structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

22. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

23. Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

24. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

25. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

26. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

27. Claims 15, 16 and 23-25 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 15, 16 and 23-25 of Application No. 10/088,950.

28. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 15, 16 and 23-25 of the instant application recite a method of preventing, inhibiting, or attenuating the differentiation of T-cells into the Th2 subtype comprising administration of an effective amount of a TCCR polypeptide or agonist thereof (Claim 15); wherein the preventing, inhibiting, or attenuating occurs in a mammal (Claim 16); wherein the agonist is a monoclonal antibody (Claim 23); wherein the antibody has nonhuman complementarity determining region (CDR) residues and human framework (FR) residues (Claim 24); and wherein the agonist is an antibody fragment, or a single-chain antibody (Claim 25). In Application No. 10/088,950, the claims recite a method of preventing, inhibiting, or attenuating the differentiation of T-cells into a Th2 subtype comprising administering an effective amount of an anti-TCCR agonist antibody (Claim 15); wherein the preventing, inhibiting, or attenuating occurs in a mammal (Claim 16); wherein the agonist is a monoclonal antibody (Claim 23); wherein the antibody has nonhuman complementarity determining region (CDR) residues and human framework (FR) residues (Claim 24); and wherein the agonist is an antibody fragment, or a single-chain antibody (Claim 25). Therefore it would be obvious that the method of preventing, inhibiting, or attenuating the differentiation of T-cells into the Th2 subtype comprising administration of an effective amount of a TCCR polypeptide or agonist thereof; and wherein the agonist is a monoclonal antibody, in claims 15, 16 and 23-25 of the instant

application would encompass the method and monoclonal antibody recited in claims 15, 16 and 23-25 of Application No. 10/088,950.

29. This is a provisional obviousness-type double patenting rejection.

30. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

31. No claim is allowed.

32. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jo Ann Rinaudo whose telephone number is 571.272.8143. The examiner can normally be reached on M-F, 8:30AM - 5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571.272.0841. The fax phone number for the organization where this application or proceeding is assigned is 571.273.8300.

33. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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10/26/2005

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